goitre. In some of the well reported instances of this disease, the ingestion of over 60 Cal. per kilo per day (double the normal amount), was not sufficient to maintain the combustions without the loss of body fat. This is a positive exaggeration, due to a positive stimulation of the reactions of combustion, and not the result of an exaggerated heat dissipation. A marked exaggeration in the combustion of fat occurs in diabetes, as a compensation to the almost complete cessation in the combustion of sugar. A moderate excess of combustion has been observed in some case of pernicious anemia and leukemia, as well as in the cachexia of malignant disease. For most other diseases there have been no investigations.

It is apparently a rule that when either the carbonous or the nitrogenous catabolism is exaggerated, the reciprocal efficiency of the other is lowered, an excess of protein in the diet will not reduce the carbon combustions as in the normal, an excess of sugar or fat will not spare protein as in the normal. Just the opposite of this is to be observed during convalescence from disease (and in subnutrition), here the saving power of carbohydrate for protein and the reciprocal availability of protein for sugar and fat are increased.

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## THE SPIROCHETA PALLIDA.*

By SANFORD BLUM, M. D., San Francisco.

THE spirocheta pallida was first recognized by Schaudin in a smear preparation obtained from a secondary syphilitic papule in March, 1905. The preparation was examined fresh and the spirocheta was first observed in its motile state. Subsequently Schaudin and Hoffmann succeeded in staining the organism and studied it also in the colored preparation. Since then various investigators have studied this interesting organism and valuable information has been contributed by Lowenthal, Metchinkoff and Roux, Buschka and Fisher and others.

Up to the present time the spirocheta pallida has been found in syphilitic subjects in the discharge from eroded primary and secondary lesions, in the deep unexposed portions of primary and secondary lesions, in smears obtained from extirpated luetic inguinal glands and from the sap obtained from luetic inguinal glands by aspiration, in deep tissue smears from isolated intact papules, in the fluid contained in pemphigus vescicles in a child congenitally luetic, in smears from the liver and spleen of a child dying from hereditary lues, and perhaps in the blood taken from the finger of a luetic individual. It has not been found except in luetic cases.

Morphologically the spirocheta pallida is a small, delicate, corkscrew-like spiral with tapering ends. It varies in length from 3 mu to 14 mu and its thickness may be estimated at ¼ mu. Each spirocheta has from 3 to 14 twists or coils. It is extremely faintly refractive and takes stains with difficulty. In life it moves rapidly by a rotary motion in the direction of its long axis. First it moves in one direction; then comes to a standstill and then moves in the opposite direction. Schaudin describes other movements which it executes without locomotion, which he ascribes to an expression of the play of an undulating membrane. These are undulatory motions involving the entire structure.

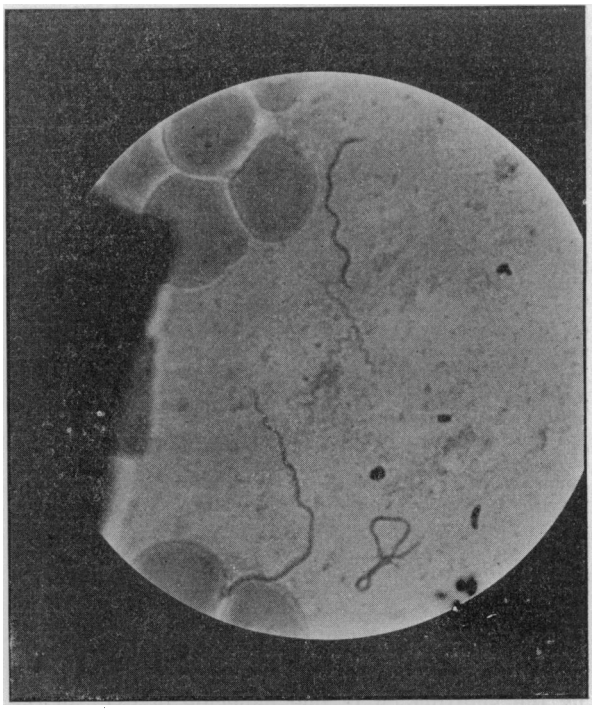
In life the spirocheta pallida differs from other spirocheta in its smallness, delicacy and much fainter refraction of light, and especially in the nature of its coils. These can best be described as corkscrew-like. They are regular, narrow and deeply bent and these characteristics are constant, whatever the source of the individual specimen may be (primary lesion, gland, papule, monkey, etc.). They have the same configuration in the stained as in fresh preparations and it may be added that they stain faintly. They do not take most of the ordinary stains and when they stain they do so more faintly than the other spirochetæ.

The technic of staining as given by Hoffman is as follows:

(1) Make a thin smear and dry in the air; (2) fix the preparation in absolute alcohol (preferably without delay); (3) dry, and stain with Giemsa's mixture. (Hoffmann uses Grübler's preparation. Of this 10-15 drops are added to 10cc distilled water. In this the preparation is stained for an hour in a porcelain dish.); (4) dry in the air and affix to slide with cedar oil or Canada balsam.

Gonder and Hoffmann succeeded in staining with fuchsin and Anilin water gentian violet.

Schaudin believes that the spirocheta family differs from the spirillum family in that the spirocheta are protozoa, while the spirilla are bacteria. He differentiates the spirocheta pallida from the other spirocheta—sp. refringens; sp. balanoposthitis; sp. erosiva circinata; sp. buccalis; sp. angina Vincenti; Anserina, Chicken, and Obermeieri—by their smallness, their greater delicacy, the nature of their spirals, their much feebler refractibility and the difficulty with which they take stains.



Microphotograph showing the delicate spirocheta pallida and also the coarser spirocheta refringens.

The cases in which Schaudin and Hoffmann found the spirocheta pallida were recent cases—4½ to 5 months old. In one instance Hoffmann found the spirocheta pallida in the blood obtained by puncturing the spleen of a man with recent lues a day before the roseola appeared. Drs. Buschka and Fisher found it in the spleen of a child dying from hereditary lues. It has also been reported as found in blood taken from the finger of a luetic individual. Schaudin found it in the pemphigus vesicles, liver and spleeen of a child afflicted with hereditary syphilis. Metchnikoff and Roux found it in the primary lesions of inoculated monkeys.

The work of Lowenthal is important. He found 9 intracellular spirocheta in one cell in the deep tissues

*A resume of investigations to date, with demonstration of specimen, before the California Academy of Medicine, August, 1905.

of a primary lesion. Also he found spirocheta in two cases in papules, isolated, intact and distant from the genital organs (in one case in a papule over the deltoid muscle). He believes the length of individual organisms is only 3 or 4 mu and that the reported long examples are really several individuals placed end to end. He also believes that mercury makes them shorter and, whereas Schaudin and Hoffmann found them only in untreated cases, he found them in cases where mercury had been used.

L. Michaelis believes that he has seen nuclei in spirochetæ pallidæ.

Note—The microphotograph was obtained from a smear preparation of the discharge from a moist papule in a case of fresh lues. It shows the frail, delicate spirocheta pallida, as well as the decidedly coarser spirocheta refringens. Magnification 1900.

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# THE RELATION OF BACTERIA TO THE DEVELOPMENT OF GALL-STONES—A REPORT OF EXPERIMENTAL STUDIES, WITH A REVIEW OF THE LITERATURE.*

By AUGUST JEROME LARTIGAU, San Francisco.

THE results of recent experimental studies upon the relation of bacteria to the formation of gall-stones have been sufficiently striking to justify newer points of view of the pathogenesis of this disease. It is now definitely known that the phenomena involved in the development of cholelithiasis are closely related to bacterial infection of the gall-bladder. However, the idea that the lesion is one dependent on local changes in the gall-bladder is not new. Indeed, in 1845, Budd suggested that the cholesterin of gall-stones might be derived from the mucous membrane of the gall-bladder; and later, Meckel von Hemsbach, in his well-known work on lithogenic catarrh, pointed out that inflammatory changes within the gall-bladder, were more or less closely associated with the formation of calculi. The increased secretion of mucus and the desquamation of epithelial cells were, to his mind, important factors in the etiology.

In 1886 Galippe[1] demonstrated the presence of micro-organisms in salivary calculi; from this observation he advanced the theory that bacteria were the essential factors in the pathogenesis of all forms of lithiasis. Five years later, at the Congress of Wiesbaden, Naunyn,[2] partly from the studies of others and partly from his own observations, strongly supported the bacterial conception of cholelithiasis.

Dupré,[3] in 1891, studied the subject of biliary infections and noted the frequent occurrence of bacteria in connection with gall-stones; from this he drew the conclusion that calculi predisposed to biliary infection. Letienne,[4] on the other hand, from more or less similar investigations, reached the conclusion that the growth of bacteria within the gall-bladder does not necessarily give rise to clinical symptoms, although it may produce a precipitation of bile elements. He did not accept the view advanced by Galippe.

[1] Galippe: Mode de formation du tartre et des calculs salivaires; considérations sur la production des calculs en général; presence des microbes, ou de leurs germes dans ces concrétions. Journ. des Connaissances Médicales, March 25, 1886; Bull. de la Soc. de Biologie, 1886; Journ. des Connaissances Médicales, 1894, p. 154.

[2] Naunyn: Die Gallensteinkrankheiten. Tenth Congress for Internal Medicine, Wiesbaden, 1891; Verhandlungen des Congresses fur Innere Medicin, Leipzig, 1892.

[3] Dupré: Les infections biliare. Thèse de Paris, 1891.

[4] Letienne: De la bile a l'état pathologique. Thèse de Paris, 1891.

[5] Charrin and Roger: Note sur l'action antiseptique de la bile. Bull. de la Soc. de Biologie, Aug. 7, 1886.

[6] Copeman and Winston: Observations on Human Bile Obtained from a Case of Biliary Fistula. Jour. of Physiology, 1889.

[7] Corrado: Sul passagio dei germi nella bile et nel contenuto enterico e sulf'azione che resontono. Ann. del Instituto d'hygiene Sperimento del Prof. Celli, 1890.

* Read at the Thirty-fifth Annual Meeting of the State Society, Riverside, April, 1905.

*The Experimental Development of Gall-Stones.*—At first glance it is surprising that, at this time, so few observers recognized the significance of Galippe's findings. This is in part accounted for by the fact that bile was generally regarded as a secretion which possessed marked germicidal properties. But Charrin and Roger,[5] Copeman and Winston,[6] Corrado,[7] and a host of others showed that bile exerted scarcely any appreciable effect on the growth of bacteria. Furthermore, as the bacterial etiology of cholecystitis was developed by the investigations of Gilbert and Dominici[8] and many others, and as the demonstration of bacteria was frequently made within gall-stones or the gall-bladders containing them, by the studies of Welch,[9] Dupré,[10] Letienne,[11] Gilbert and Dominici,[12] and Gilbert and Fournier,[13] the theory of the casual relationship of bacteria to cholelithiasis came more prominently into the foreground, and has gradually been developed by several investigators, who have induced the formation of calculi in animals. Gilbert and Dominici[14] state that they had observed in 1893 the presence of "petites concrétions vérdatres" in a case of experimental typhoid cholecystitis. Following this observation, systematic attempts were made to obtain gall-stones experimentally. Thus, Fournier[15] made a series of studies with this object in view, but was unsuccessful. Later, in January, 1897, Gilbert,[16] with Fournier, obtained a stone from the gall-bladder of a dog which had been previously inoculated with the bacillus coli communis.*

The first comprehensive experimental work along these lines was undertaken by Mignot, who communicated the first results[17] of his investigations to the French Society of Surgery, Paris, in May, 1897.

He showed several stones obtained in guinea pigs by direct inoculations of the bacillus coli communis into the gall-bladder. In the following year,[18] he published the results of his more extended studies. By the direct inoculation of various bacteria—bacillus coli communis, bacillus typhosus, bacillus subtilis, staphylococcus and streptococcus—into the gall-bladder of animals, calculi were obtained. He especially insisted upon the fact that for the experimental development of gall-stones it is essential that the organisms be of attenuated virulence.

It was formerly thought that foreign bodies played an important role in the formation of calculi. Very often in the center of gall-stones masses of epithelial cells and bacteria are found; less often blood clots, worms, needles, globules of mercury, plum stones, or suture material, as in the cases reported by Homans and Kehr.

Mignot, therefore, studied the significance of inert foreign bodies in the formation of stones. He introduced into the gall-bladder sterile silk thread, bits of cotton, and hard substances, such as fragments of human calculi. So long as the gall-bladder remained free from bacterial inflammation no stones were formed. Then, to show that the negative results obtained were not due to an absence of bile stagnation,

[8] Gilbert and Dominici: Angiocholite et cholécystites typhiques expérimentales. Bull. de la Soc. de Biologie, Dec. 23, 1893; Angiocholite et cholécystite cholériques expérimentales. Ibid. Jan. 13, 1894; Angiocholite et cholécystite colibacillaires expérimentales. Ibid. Jan. 20, 1894; Sur l'infection expérimentale des voies biliares par le stréptocoque, le staphylocoque doré, et le pneumocoque. Ibid. Feb. 24, 1894.

[9] Welch: The Bacillus Coli Communis: the conditions of its invasion of the human body and its pathogenic properties. Med. News, vol. LIX, 1891.

[10] Dupré: Loc. cit.

[11] Letienne: Loc. cit.

[12] Gilbert and Dominici: La lithiase biliare ést-elle de nature microbiennes? Bull de la Soc. de Biologie, June 16, 1894.

[13] Gilbert and Fournier: Du role des microbes dans la genèse des calculs biliares. Bull. de la Soc. de Biologie, Feb. 8, 1896.

[14] Gilbert and Dominici: Loc. cit.

[15] Fournier: L'origine microbienne de la lithiase biliare. Thèse de Paris, 1896.

[16] Gilbert: Note pour servir a l'historie de la théorie microbienne de la lithiase biliare. Arch. Gén. de Méd., vol. II, Sept. 1898.

[17] Mignot: Calculs biliares expérimentaux. Soc. de Chirurgie, May 10, 1897.

[18] Mignot: L'origine microbienne des calculs biliares. Arch. Gén. de Méd., vol. II, 1898.

* Although published after Mignot's communication, Gilbert and Fournier were probably the first to experimentally obtain gall-stones.